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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

M3591N

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

WARNING LETTER
VIA EXPRESS

DEC 9 1999

Mr. Per Mulbjerg
Plant Manager
Codan Medical APS
Faergevej 4
Rodby, Denmark DK-4974

Dear Mr. Mulbjerg:

During an inspection of your firm located in Rodby, Denmark, on October 4-7, 1999, our investigator determined that your firm manufactures syringes. These products are devices as defined by Section 201(h) of the Federal, Food, Drug, and Cosmetic Act (the Act).

The above-stated inspection revealed that these devices are adulterated within the meaning of Section 501(h) of the Act, in that the methods used in, or the facilities or controls used for manufacturing, packing, storage, or installation are not in conformance with the Quality System Regulation, as specified in Title 21, Code of Federal Regulation (CFR), Part 820, as follows:

1. Failure to establish and maintain procedures to ensure that formal documented reviews of the design results are planned and conducted at appropriate stages of the device's design development, as required by 21 CFR 820.30(e). For example, the Design Control/Change Control procedures do not include procedures for design reviews.

2. Failure to establish and maintain procedures for defining and documenting design output in terms that allow an adequate evaluation of conformance to design input requirements, as required by 21 CFR 820.30(d). For example, the Design Control/Change Control procedures do not include procedures for defining and documenting design output in terms that allow an adequate evaluation of conformance to design input requirements.

3. Failure to establish and maintain procedures for verifying the device design, as required by 21 CFR 820.30(f). For example, procedures for verifying design outputs meet design inputs were not established.

4. Failure to establish and maintain procedures for validating the device design, as required by 21 CFR 820.30(g). For example, the Design Control/Change Control procedures do not include procedures for validating the device design.

5. Failure to validate with a high degree of assurance a process that cannot be fully verified by subsequent inspection and test, as required by 21 CFR 820.75(a). For example, no validation had been conducted for the sterilization cycle parameters used for daily sterilization runs.

6. Failure to review and evaluate a process and adequately perform revalidation when process deviations occur, as required by 21 CFR 820.75(c). For example:

   a. no validation exists for the resterilization of products that had to be resterilized due to positive BI results; and
   b. a change was made to the mold used to make the seal ring for the syringes; however, there was no documentation to ensure revalidation was done adequately, or even performed at all.

7. Failure to establish and maintain procedures for rework, to include retesting and reevaluation of the nonconforming product after rework, to ensure that the product meets its current approved specifications, as required by 21 CFR 820.90(b)(2). For example, no specifications exist for the resterilization of products and/or the number of resterilization cycles permitted for each lot.

8. Failure to adequately document the investigation of any complaint involving the possible failure of a device to meet any of its specifications, as required by 21 CFR 820.198(e). For example, investigations of the following complaints were not fully documented:

   - Complaint [redacted]
   - Complaint [redacted]
   - Complaint [redacted]

9. Failure to establish procedures for review of the suitability and effectiveness of the quality system to ensure that the quality system satisfies the requirements of this part and the established quality policy and objectives, as required by 21 CFR 820.20(c). For example, procedures for management reviews were not defined or documented.

10. Failure to establish and maintain procedures for implementing corrective and preventive actions, which include verifying or validating the corrective and preventive action to ensure that such action is effective and does not adversely affect the finished device, as required by 21 CFR 820.100(a)(4). For example, corrective and preventive action procedure, [redacted], fails to require verification or validation of changes.

11. Failure to define and require the use of appropriate statistical methodology where necessary to detect recurring quality problems, as required by 21 CFR 820.100(a)(1). For example, corrective and preventive action procedure, [redacted], fails to define and require the use of appropriate statistical methodology to identify existing and potential causes of non-conforming product.

12. Failure to adequately establish a quality plan which defines the quality practices, resources, and activities relevant to the devices that are designed and manufactured, as required by 21 CFR 820.20(d). For example:

    a. the quality plan/program was not defined; and
    b. the quality plan is not complete, in that there is no requirement that adequate resources be provided for performance of work assessment activities.

13. Failure to ensure and document that all inspection and test equipment is suitable for its intended purposes and is capable of producing valid results, as required by 21 CFR 72(a). For example, with respect to Complaint [redacted], there was no documentation to show that the automatic detection system used to detect defective syringes, was operating correctly.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Act and regulations. The specific violations noted in this letter and in the form FDA 483 issued at the conclusion of the inspection may be symptomatic of serious underlying problems in your firm's manufacturing and quality assurance system. You are responsible for investigating and determining the causes of the violations identified by the Food and Drug Administration. If the causes are determined to be systems problems, you must promptly initiate permanent corrective actions.

We acknowledge receipt of your October 20, 1999, response to the FDA 483. However, our review indicates that it is inadequate in that you did not provide documentation to demonstrate that you have corrected the noted observations.

Federal agencies are advised of the issuance of all Warning Letters about devices so that they may take this information into account when considering the award of contracts. Given the serious nature of these violations of the Act, all syringes manufactured by Codan Medical APS of Rodby, Denmark may be detained upon entry into the United States (U.S.) until these violations are corrected.

In order to remove the devices from this detention, it will be necessary for you to provide a written response to the charges in this Warning Letter for our review. After we notify you that the response is adequate, it will be your responsibility to schedule an inspection of your facility. As soon as the inspection has taken place, and the implementation of your corrections have been verified, your products may resume entry into this country.

Please notify this office in writing within 15 days of the specific steps you have taken to correct the noted violations, including an explanation of each step being taken to identify and make correction to any underlying systems problems necessary to assure that similar violations will not recur. Please include any and all documentation to show that adequate correction has been achieved. In the case of future corrections, an estimated date of completion, and documentation showing plans for correction, should be included with your response to this letter.

If documentation is not in English, please provide an English translation to facilitate our review. Please address your response and any questions to the Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Enforcement II, General Hospital Devices Branch, HFZ-333, 2098 Gaither Road, Rockville, Maryland 20850, to the attention of Ms. Carolyn Niebauer.

Should you require any assistance in understanding the contents of this letter, do not hesitate to contact Ms. Leslie E. Dorsey at the letterhead address or at (301) 594-4618 or FAX (301) 594-4638.

Sincerely yours,

James L. Work Jr

Lillian J. Gill
Director
Office of Compliance
Center for Devices and
Radiological Health